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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/814,002	03/30/2004	Balram Ghosh	206,487	6062

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1637	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/814,002	GHOSH ET AL.	
	Examiner	Art Unit	
	STEPHANIE K. MUMMERT	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 October 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *105,107,110 and 117-119* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *105,107,110 and 117-119* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment filed on October 14, 2008 is acknowledged and has been entered. Claims 105, 110 and 118 have been amended. Claims 1-104, 106, 108-109, 111-116, and 120 have been canceled. Claims 105, 107, 110 and 117-119 are pending.

Claims 105, 107, 110 and 117-119 are discussed in this Office action.

All of the amendments and arguments have been thoroughly reviewed and considered but are not found persuasive for the reasons discussed below. Any rejection not reiterated in this action has been withdrawn as being obviated by the amendment of the claims. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

This action is made FINAL.

Previous Rejections

The rejection of claims 105, 110, 117-119 as being vague and indefinite is withdrawn in view of Applicant's amendment to the claims.

Claim Interpretation

The term 'R1 allelic variant' and 'R3 allelic variant' are not clearly defined in the claims and instead are referred to as allelic variants. The R1 term is not explicitly defined, but is described as "The SEQ ID No. 1 has 1-392 contiguous nucleotides containing one or more group

of GT dinucleotide polymorphisms at positions from 125 to 168 of R1 locus" (previous claim 1 and throughout specification, including paragraph 58 of PgPub). The R3 term is not explicitly defined, but is described as "the SEQ ID No.2 has 1 to 336 contiguous nucleotides containing one or more group of GT dinucleotide polymorphisms at positions from 87 to 116 bases of R3 locus" (previous claim 1 and throughout specification, including paragraph 59 of PgPub). Therefore, the term R1 variant is being interpreted as reading on nucleotides 125-168 of SEQ ID NO:1 comprising a GT repeat region and the term R3 variant is being interpreted as reading on nucleotides 87-116 of SEQ ID NO:2 comprising a GT repeat region.

Furthermore, limitations regarding intended use of the nucleic acids, including use in predicting susceptibility of a subject to asthma, or association of the sequences (or their haplotypes) with specific diseases are not interpreted as imposing a structural limitation on the nucleic acid. The nucleic acids as claimed are capable of performing the intended use and would therefore also be capable of being associated with these individual diseases. Therefore nucleic acids that meet the structural limitations of the nucleic acids claimed are interpreted as anticipating the invention as claimed.

Claim Rejections - 35 USC § 102

1. Claims 105, 107 and 118-119 are rejected under 35 U.S.C. 102(b) as being anticipated by Patel et al. (Genomics, 1998, vol. 52, p. 192-200). Patel teaches the mapping and characterization of the human STAT6 gene (Abstract).

With regard to claim 105, Patel teaches an isolated R1 allelic variant consisting of GT dinucleotide repeats from the nucleotide position 125 from 5' end of SEQ ID NO: 1 of Signal Transducer and Activator of Transcription-6 (STAT-6) gene for use in predicting susceptibility of a human subject to atopic asthma (see attached sequence alignment, HSSTATSIX1, specifically nucleotides 908-1299, which comprises SEQ ID NO:1 and the repeat region R1, located at nucleotides 1032-1074 of Patel or nucleotides 125-167 of SEQ ID NO:1 below, which consists of GT dinucleotide repeats from nucleotide position 125 from 5' end of SEQ ID NO:1 and where the sequence source is human),

```
Qy        121 AATCGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGACGGAGTCTTG 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1028 AATCGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGACGGAGTCTTG 1087
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With regard to claim 107, Patel teaches an isolated R3 alellic variant consisting of GT dinucleotide repeats from nucleotide position 87 from the 5' end of SEQ ID NO: 2 of Signal Transducer and Activator of Transcription-6 (STAT-6) Gene for use in predicting susceptibility of a human subject to atopic asthma (see attached sequence alignment, HSSTATSIX1, specifically nucleotides 3605-3940, which comprises SEQ ID NO:2 and the repeat region R3, located at nucleotides 3691-3720 of Patel or nucleotides 87-116 of SEQ ID NO:2 below, which consists of GT dinucleotide repeats from nucleotide position 87 from 5' end of SEQ ID NO:2, where the sequence source is human).

```
Qy         61 CACTGAAGAGGGAGGACGGGAGAGGAGTGTGTGTGTGTGTGTGTGTGTGTGTATGT 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       3665 CACTGAAGAGGGAGGACGGGAGAGGAGTGTGTGTGTGTGTGTGTGTGTGTGTATGT 3724
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With regard to claim 118, Patel teaches an isolated pharmacogenetic marker having SEQ ID NO: 1 (see attached sequence alignment, HSSTATSIX1, specifically nucleotides 908-1299,

which comprises SEQ ID NO:1 and the repeat region R1, located at nucleotides 1032-1074 of Patel or nucleotides 125-167 of SEQ ID NO:1 above) and 2 (see attached sequence alignment, HSSTATSIX1, specifically nucleotides 3605-3940, which comprises SEQ ID NO:2 and the repeat region R3, located at nucleotides 3691-3720 of Patel or nucleotides 87-116 of SEQ ID NO:2 above) for detecting and predicting a predisposition to atopic asthma of STAT-6 gene in a human subject (see attached HSSTATSIX1 alignment, and the teaching of Patel, where the sequence source is human).

With regard to claim 119, Patel teaches an isolated pharmacogenetic marker according to claim 118, wherein SEQ ID NO. 1 is associated with R1 locus (see attached sequence alignment, HSSTATSIX1, specifically nucleotides 908-1299, which comprises SEQ ID NO:1 and the repeat region R1, located at nucleotides 1032-1074 of Patel or nucleotides nucleotides 125-167 of SEQ ID NO:1 above) and SEQ ID No. 2 is associated with R3 locus of STAT-6 gene (see attached sequence alignment, HSSTATSIX1, specifically nucleotides 3605-3940, which comprises SEQ ID NO:2 and the repeat region R3, located at nucleotides 3691-3720 of Patel or nucleotides 87-116 of SEQ ID NO:2 above).

2. Claims 105, 107, 110 and 117-119 are rejected under 35 U.S.C. 102(a) as being anticipated by Nagarkatti et al. (Journal of Human Genetics, 2002, vol. 47, p. 684-687). Nagarkatti teaches the identification of three polymorphic (CA) repeat regions and the examination of allelic frequency and haplotypes was conducted (Abstract).

With regard to claim 105, Nagarkatti teaches an isolated R1 allelic variant consisting of GT dinucleotide repeats from the nucleotide position 125 from 5' end of SEQ ID NO: 1 of

Signal Transducer and Activator of Transcription-6 (STAT-6) Gene for use in predicting susceptibility of a subject to atopic asthma (see attached sequence alignment, HSSTATSIX1, which matches accession number AH006951 referenced p. 685, col. 1, specifically nucleotides 908-1299, which comprises SEQ ID NO:1 and the repeat region R1, located at nucleotides 1032-1074 of Nagarkatti or nucleotides 125-168 of SEQ ID NO:1 below; also see Table 1, 'STAT6 gene' heading)

```
Qy        121 AATCGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGACGGAGTCTTG 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1028 AATCGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGACGGAGTCTTG 1087.
```

With regard to claim 107, Nagarkatti teaches an isolated R3 alellic variant consisting of GT dinucleotide repeats from nucleotide position 87 from the 5' end of SEQ ID NO: 2 of Signal Transducer and Activator of Transcription-6 (STAT-6) Gene for use in predicting susceptibility of a subject to atopic asthma (see attached sequence alignment, HSSTATSIX1, which matches accession number AH006951, specifically nucleotides 3605-3940, which comprises SEQ ID NO:2 and the repeat region R3, located at nucleotides 3691-3720 of Nagarkatti or nucleotides 87-116 of SEQ ID NO:2 below; also see Table 1, 'STAT6 gene' heading).

```
Qy          61 CACTGAAGAGGGAGGACGGGAGAGGAGTGTGTGTGTGTGTGTGTGTGTGTGTATGT 120
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        3665 CACTGAAGAGGGAGGACGGGAGAGGAGTGTGTGTGTGTGTGTGTGTGTGTGTATGT

3724
```

Regarding claim 110 and 117, while the inclusion of specific haplotypes imposes a structural limit on the number of CA repeats present in the sequence comprising SEQ ID NO:1 and 2, the limitations regarding specific p values does not impose a structural limitation on the nucleic acid sequence. Therefore, the claims are rejected solely on the basis of specific haplotypes disclosed by Nagarkatti.

With regard to claim 110, Nagarkatti teaches an isolated allelic variant according to claim 105, wherein haplotypes 17_15 (CA repeat 17 on R1 locus and 15 on R3 locus of the STAT-6 gene having a 'p' value less than 0.0031 and 16_15 (CA repeat 16 on R1 locus and 15 on R3 locus of the STAT-6 gene having a p value less than 0.001 associated with susceptibility to asthma (Table 2, where haplotypes comprising 17_15 were identified in the STAT-6 gene; Table 2, where haplotypes comprising 16_15 were identified in the STAT-6 gene).

With regard to claim 117, Nagarkatti teaches an isolated allelic variant according to claim 105, wherein haploypes 17__14 (CA repeat 17 on R1 locus and 14 on R3 locus of the STAT-6 gene having a 'p' value less than 0.00001), 23__16 (CA repeat 23 on R1 locus and 16 in R3 locus of the STAT- 6 gene having a 'p' value less than 0.00001) and 24 16 (CA repeat 24 on R1 locus and 16 in R3 locus of the STAT-6 gene having a 'p' value less than 0.0001) are associated with protection from asthma (Table 2, where haplotypes 24_16 were identified in the STAT-6 gene; see also p. 686, col. 1, where it is noted that Table 2 represents 76% of all haplotypes and others were not included).

With regard to claim 118, Nagarkatti teaches an isolated pharmacogenetic markers having SEQ ID NOS: 1 (see attached sequence alignment, HSSTATSIX1, which matches accession number AH006951 referenced p. 685, col. 1, specifically nucleotides 908-1299, which comprises SEQ ID NO:1 and the repeat region R1, located at nucleotides 1032-1074 of Nagarkatti or nucleotides 125-168 of SEQ ID NO:1 above; also see Table 1, 'STAT6 gene' heading) and 2 (see attached sequence alignment, HSSTATSIX1, which matches accession number AH006951, specifically nucleotides 3605-3940, which comprises SEQ ID NO:2 and the repeat region R3, located at nucleotides 3691-3720 of Nagarkatti or nucleotides 87-116 of SEQ

ID NO:2 above; also see Table 1, 'STAT6 gene' heading) for detecting and predicting a predisposition to atopic asthma of STAT-6 gene in a human subject.

With regard to claim 119, Nagarkatti teaches an isolated pharmacogenetic markers according to claim 118, wherein SEQ ID NO. 1 is associated with R1 locus (see attached sequence alignment, HSSTATSIX1, which matches accession number AH006951 referenced p. 685, col. 1, specifically nucleotides 908-1299, which comprises SEQ ID NO:1 and the repeat region R1, located at nucleotides 1032-1074 of Nagarkatti or nucleotides 125-168 of SEQ ID NO:1 above; also see Table 1, 'STAT6 gene' heading) and SEQ ID No. 2 is associated with R3 locus of STAT-6 gene (see attached sequence alignment, HSSTATSIX1, which matches accession number AH006951, specifically nucleotides 3605-3940, which comprises SEQ ID NO:2 and the repeat region R3, located at nucleotides 3691-3720 of Nagarkatti or nucleotides 87-116 of SEQ ID NO:2 above; also see Table 1, 'STAT6 gene' heading).

Relevant Prior Art

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Nyce et al. (WO0062736; October 2000) discloses oligonucleotide compositions for prophylactic, preventive and therapeutic treatments associated with impaired respiration, lung allergies and/or inflammation and discloses sequences of STAT6 (Abstract and attached alignments).

Response to Arguments

3. Applicant's arguments filed October 14, 2008 have been fully considered but they are not persuasive.

In the instant response, Applicant traverses the rejection of claims under Patel and states, "all of the claims 105, 107, 110 and 117-119 are patentable over Patel and Nagarkatti" (p. 4 of remarks).

Applicant argues "Patel does not describe the Stat6 gene sequence being used to predict susceptibility of a human subject to atopic asthma" and "neither GA nor GT repeating nucleotide sequences are the subject of this article". Applicant also argues "Patel reference does not show the requirements of claims 105 and 107" and "there is no mention of isolated pharmacogenetic markers in the Patel reference required by claims 118-119" (p. 5 of remarks).

Applicant's arguments do not comply with 37 CFR 1.111(c) because they do not clearly point out the patentable novelty which he or she thinks the claims present in view of the state of the art disclosed by the references cited or the objections made. Furthermore, as Applicant has not clearly stated how the sequence of Patel distinguishes over the sequences of SEQ ID NO:1 or 2, the rejection is maintained. As stated in the art rejection above, Patel teaches the sequence of SEQ ID NO:1 and 2 and includes the R1 and R3 variants described by the GT dinucleotide repeats as amended, as beginning at position 125 of SEQ ID NO:1 and position 87 of SEQ ID NO:2. These GT dinucleotide repeats represent these allelic variants, which are part of SEQ ID NO:1 and 2 respectively. Regarding the pharmacogenetic marker, the specification does not define these markers as distinct from a composition comprising the nucleic acid sequences

themselves. Therefore, a teaching in the prior art of the sequences which meet the limitation of the "marker" is interpreted as anticipating the rejection.

In response to applicant's argument that Patel does not disclose or teach anything about asthma (referring to the use of the allelic variants in predicting susceptibility to disease), a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the limitation of the claim. Therefore, in this case, the isolated variants are the same, regardless of the intended use of the sequences in determining the susceptibility to asthma. Since Patel teaches the sequences as claimed, the rejection is anticipated.

Furthermore, regarding the lack of specific teaching that the sequences are useful in diagnosing asthma, as noted in the previous response, the limitation regarding which disease is associated with the specific gene variant does not impose a structural limitation on the sequence or structure of the nucleic acid. Therefore, these claims are rejected in view of the nucleic acid sequence, represented by HSSTATSIX1 of Patel described above with regard to claims 105 and 107. The rejection is maintained.

Applicant also notes "there is a unnumbered NCBI HSSTATSIX1 gene printed-out section of a nucleotide series which has a short caption above it which mentions asthma following the Patel article, however, there is no indication of how that section is related to the Patel article". Applicant states "this would be page 11 with 'SEQ ID NO:1' handwritten on" the top of the page" (p. 4 of remarks).

It is noted in response that this portion of the sequence alignment was attached to the end of the NCBI print out of the STAT-6 gene. The sequence alignment starting on page 11, with 'SEQ ID NO:1' handwritten at the top represents the sequence of STAT-6 in the Nyce reference, cited as relevant in the office action above. This portion of the record is not intended to draw a connection between Patel and STAT-6.

Applicant traverses the rejection of the claimed subject matter as being anticipated by Nagarkatti. Applicant argues "Nagarkatti merely describes the content of STAT6 and IL4 RA genes. It is therefore clear that association of allelic variants and specific haplotypes of STAT 6 gene described in the present invention have not been disclosed or suggested by Nagarkatti". Applicant also argues "on p. 686 of Nagarkatti, there is not any 16 15 [haplotype having] CA repeat 16 on R1 locus and 15 on R3 locus of the STAT6 gene having a p value less than 0.0001". Applicant also states "there is no disclosure or suggestion of isolated pharmacogenetic markers in Nagarkatti as required by claims 118 and 119 of the present invention" (p. 5 of remarks).

Contrary to Applicant's arguments, Nagarkatti clearly teaches a 16 15 haplotype, 17_14 haplotype and 24_16 (as claimed, not 23_16 as argued) haplotype in Table 2 on p. 686. While the p value of these haplotypes are not provided in Nagarkatti, as noted in the art rejection above, "the limitations regarding specific p values do not impose a structural limitation on the nucleic acid sequence." Changing the p value associated with the sequence would not change the structure of the sequence. Therefore, the teaching of the specific allelic sequences of STAT6, particularly in the form of haplotypes, as taught by Nagarkatti anticipates the invention as claimed. The rejection is maintained.

Conclusion

No claims are allowed. All claims stand rejected.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to STEPHANIE K. MUMMERT whose telephone number is (571)272-8503. The examiner can normally be reached on M-F, 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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